REMARKS

Amendment to the claims

Claims 43, 57 and 63 are amended herein to correct a typographical error in the original claims. SEQ ID NO: 256 is a twenty nucleobase antisense compound. In one aspect, the antisense was synthesized to include five 2'-O-methoxyethyl (2'-MOE) nucleotides at the wings (i.e., at the 5' and 3' termini) and a central region of ten deoxynucleotides. See p. 100, lines 16-21, using page numbering from the parental PCT publication WO 00/74687. Thus, nucleotides 1-5 (the 5' terminus) are modified, nucleotides 6-15 are not modified, and nucleotides 16-20 (the 3' terminus) are modified. The amendment to the claims therefore includes no new matter.

The objection to the specification

The examiner objected to the specification asserting that the abstract fails to comply with 37 CFR 1.52(b)(4) in that it does not commence on a separate sheet apart from any other text. Substitute pages of the specification are provided herewith, thereby rending moot the objection.

The rejection under 35 USC 112, first paragraph

The examiner rejected claims 31-34 and 36-49 under 35 USC 112, first paragraph, for assertedly lacking enablement for any antisense compound comprising at least eight nucleobases of SEQ ID NO: 256. Applying the Wands analysis for undue experimentation, the examiner first asserted that use of any eight nucleobases from SEQ ID NO: 256 was unpredictable, and in addressing the state of the art, amount of guidance provided by the specification, nature of the invention, and level of skill in the art, the examiner referred back to this asserted unpredictability in the art. From this analysis, the examiner concluded that "undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention." [Office Action at page 5.] The applicants respectfully disagree.

The rejected claims are directed to compounds derived from, and including, the 30 nucleobase antisense sequence set out in SEQ ID NO: 256. In making the rejection, the examiner did not argue that the worker of ordinary skill in the art could not make any and all of the claimed compounds. The examiner's silence on this issue was proper in view of the

extensive guidance provided by the specification for making the claimed compounds and the examiner's admission that the level of skill in the art is high [Office Action at page 5]. Making the claimed compounds, therefore, cannot be concluded to require undue experimentation. Instead, the examiner based the rejection on what appears to be asserted unpredictability of the usefulness of claimed compounds to inhibit B7 expression. The examiner's focus, therefore, was on the predictability of a result, and not on whether the specification teaches how to use the claimed compounds without undue experimentation.

However, whether every compound within the scope of the claims actually inhibit B7 expression is not the question. Instead, the proper analysis in this instance is whether identification of operative species within the claimed genus would require undue experimentation. Claims are not broader than the enabling disclosure even if they read on a very large number of inoperative embodiments if "a person skilled in the relevant art could determine which conceived but not-yet-fabricated embodiments would be inoperative with expenditure of no more effort than is normally required" in the art. *In re Cook*, 169 USPQ 298, 302 (CCPA 1971).

There can be no doubt that the specification teaches many ways to use any compound within the scope of the claims. Examples 2 teaches an assay to assess modulation of human B7-1 protein expression in transfected COS cells. Example 3 teaches an assay for assessing inhibition of human B7-2 protein in transfected COS cells. Example 4 describes an in vitro ribonuclease assay to assess modulation of human B7-2 mRNA. Example 7 provides an assay to assess modulation of human B7-2 expression in antigen presenting cells. Example 8 discloses an assay to assess modulation of T cell proliferation using a compound of the invention. Example 9 provides an assay to determine modulation murine B7-2 in transfected COS cells. Example 10 describes a murine model to evaluate compounds for the ability to inhibit allograft rejection. Example 16 describes an assay to evaluate the effect of compounds on human and mouse B7-1 and B7-2 cell surface expression. Example 17 provides a murine model to evaluate the compounds effect on rheumatoid arthritis. Example 18 describes a murine model to assess the effect of compounds on multiple sclerosis. Example 21 provides an assay to assess the effect of compounds in a human psoriasis model. Because of this extensive detail, the skill artisan could test the usefulness of any compound within the scope of the claims to inhibit expression of any B7 protein with expenditure of no more effort than is normally required, *i.e.*, routine experimentation.

In addition, the amount of guidance provided by the specification for using the claimed compounds renders moot any reliance by the examiner on the amount of

experimentation that may be required to identify compounds that are useful. The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *PPG Indus., Inc. v. Guardian Indus. Corp.* , 75 F.3d 1558, 1564, (Fed. Cir. 1996) (quotation and citation omitted). As shown above, the amount of guidance provided by the specification for using the claimed compounds is more than reasonable.

Accordingly, the applicants submit that the specification fully enables use of the invention commensurate with the scope of the claims and that the rejection of claims under 35 USC 112, first paragraph may be withdrawn.

The objection to claim 70

The examiner objected to claim 70 under 3 CFR 1.75 asserting that the claim was a substantial duplicate of claim 64. Cancellation of claim 70 herein renders the objection moot.

CONCLUSION

In view of the amendments and remarks made herein, the applicants believe that all pending claims are now in condition for allowance and respectfully request notification of the same.

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